

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. Claim Status and Amendments

Claims 1 and 2 were examined on the merits and stand rejected.

Claims 1 and 2 are amended to recite "An isolated microorganism" to thereby identify the product as not found in nature as suggested by the Examiner, and that the strain comprises gene groups of avernectin aglycon biosynthesis of *Streptomyces avermitilis*, e.g., as previously recited in claims 6 and 7. Claim 2 is further amended to independent form, including all of the limitations of the base claim and any intervening claims.

Claims 1-6 and 10-15 remain pending.

Claims 3-6 and 10-15 were withdrawn for being directed to non-elected subject matter. However, claims 3, 5, 6, 10, 11 and 13-15 were amended in a manner consistent with claim 1, and rejoinder of these claims is respectfully requested.

No new matter has been added.

II. Amendment to the Specification

The Specification was amended to correct unintentional translation errors at pages 3, 5, 7, 8, 23, 24 and 32 as indicated.

No new matter has been added.

III. 101 Rejection

Claim 1 was rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter (i.e., a product of nature) for the reasons on page 3 of the Office Action.

The present amendment overcomes this rejection by amending the beginning of the claims to recite "An isolated microorganism" to thereby identify the product as not found in nature. Withdrawal of the rejection is requested.

IV. Enablement Rejection

On pages 3-5, claim 2 was rejected under 35 U.S.C. § 112, first paragraph, as not being enabled for the specific strain of *Streptomyces cyaneogriseus* recited in the claim. This rejection is respectfully traversed.

To start, Applicants note that a Certificate For Microorganisms Deposit for the specific strain of *Streptomyces cyaneogriseus* FERM BP-8394 recited in claim 2 was submitted on May 17, 2005 with the application filing papers. This document is evidence that the strain was deposited under the terms of the

Budapest Treaty. See also the reference to this deposit at page 5, lines 7-16, wherein it is indicated that this deposit was made under the terms of the Budapest Treaty.

Pursuant to 37 C.F.R. § 1.808, (1) access to the deposit will be made available during pendency of the patent application making reference to the deposit to one determined by the Director to be entitled thereto; and (2) subject to paragraph (b) of 37 C.F.R. § 1.808, all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent.

The specification makes appropriate reference to the deposit information at page 5, lines 7-16, in accordance with US practice.

Therefore, the enablement rejection is untenable and should be withdrawn.

V. Obviousness Rejection

On pages 5-6, claim 1 was rejected under 35 U.S.C. § 103(a) as obvious over Carter (J. Antibiot., vol. 41, no. 4, pp. 519-529 (1988)) in view of MacNeil (US 5,312,753) and Huang (US 2005/0003409). This rejection is respectfully traversed.

The primary reference of Carter was relied upon for disclosing a strain of *Streptomyces cyaneogriseus* subspecies *noncyanogenus* that produces nemadectin. Carter is the original

report of the discovery of nemadectin. Carter includes disclosures as to the cultivation of the producing bacterium, extraction, purification and analysis of the structure. However, Carter fails to disclose or suggest the specific microorganism strains of the invention.

The Office relied upon MacNeil as disclosing a related strain of *Streptomyces* that produces a related C-13 glycosylated nemadectin product. While MacNeil does disclose a strain of *Streptomyces avermitilis* which glycosylates avermectin compounds, there is no disclosure of any strain belonging to the *Streptomyces cyaneogriseus* sub-species *noncyanogenus* as used in the present invention. MacNeil refers to possible glycosylation at 4'-, 13- or 14a-positions. To the extent that this reference refers to reaction at the 13-position, however, there is no suggestion that stereoselectivity is obtained at the 13-position. Thus, for example, in claim 1 of MacNeil the formulae on pages 37 and 38 show glycosylation at C-13 in a non-stereospecific manner (joined using the conventional wavy line). Thus, MacNeil neither suggests use of the specific type of microorganism used in the invention nor does it obtain the stereoselective synthesis provided by the invention.

Huang relates to the cloning of the entire metabolic pathway of nemadectin and related products, but Huang does not suggest that the strain in Carter has the ability to produce C-13 glycosylated nemadectin. Further, there is no suggestion in any

reference to alter the strain in Carter to produce a strain capable of producing C-13 glycosylated nemadectin. The rejection appears to employ improper hindsight reconstruction to arrive at the claimed strain.

For these reasons, it is believed that claim 2 is novel and non-obvious over the combination of Carter in view of MacNeil and Huang. Withdrawal of the rejection is requested.

V. IDS

Most of cited references from the IDS filed May 17, 2005 were not considered. The position of the Official Action was that these references were not provided to the Office. However, these references should have been provided to the Patent Office, as these references were cited in the international application from which the present application is a National Phase. Applicants have provided a courtesy copy of these references in the appendix of this amendment.

V. Conclusion

Having addressed all the outstanding issues, the amendment is believed to be fully responsive. In view of the above, it is respectfully submitted that the application is in condition for allowance and notice to that effect is hereby requested. If the Examiner has any comments or proposals for

expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Robert A. Madsen/
Robert A. Madsen, Reg. No. 58,543
209 Madison Street, Suite 500
Alexandria, VA 22314
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

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APPENDIX:

The Appendix includes the following item(s):

-WO 93/18779.

-JP 2003-33188 (Abstract).

-NAKAGAWA, K. et al., MICROBIAL CONVERSION OF MILBEMYCINS:

HYDROXYLATION OF MILBEMYCIN A4 AND RELATED COMPOUNDS BY

Cunninghamella echinulata ATCC 9244. J. Antibiot., 1991, Vol.

44, No. 2, pages 232 to 240.

- Haruo IKEDA et al., Combinatorial Biosynthesis-Polyketide Kogobutsu

o Rei to shite-", Protein, Nucleic acid and Enzyme, Vol. 43,

No. 9, (1998), pages 1265 to 1277.

-Haruo IKEDA et al., "Metabolic Engineering no Tenkai-1 Biseibutsu

2ji Taisha Sanbutsu Seigosei no Kinoteki Kakuhon ni yoru Yuyo

Bushitsu no Sangyo", Kagaku to Seibutsu, Vol. 34, No. 11,

(1996), pages 761 to 771.

-Haruo IKEDA et al., "Series Taisha Kogaku/Seigosei Kogaku (4)

Seigosei (2) Hosenkin Polyketide Segosei Idenshi no Kaiseki to

sono Oyo", Bioscience & industry, Vol. 59, No. 8, (2001),

pages 530 to 533.

-MACNEIL D.J. et al., A Comparison of the Genes Encoding the

Polyketide Synthases for Avermectin, Erythromycin, and

Nemadectin. Ind. Microorg. (Edited by BALTZ R.H. et al.),

1993, pages 245 to 256.

-SHIH T.L. et al., SYNTHESIS OF AN AVERMECTIN-NEMADECTIN HYBRID.

Tetrahedron Lett., 1991, Vo.32, No.30, pages 3663 to 3666